Modeling Initiatives at HHS
Update to the Secretary's Council

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- ORDC is currently involved in two major modeling initiatives
  - Smallpox
  - Anthrax
- To evaluate the relative efficacy of medical and public health consequence management strategies to bioterrorist attacks
- To assist in determination of requirements and options for procurement of biodefense countermeasure products under BioShield

- Chair of Working Groups: Dr. Chin
- To date findings of Smallpox Modeling Working Group
- Preliminary findings of Anthrax Modeling Working Group

Smallpox

- Phase 1: Completed
  - Small
  - Medium
- Phase 2: Ongoing
  - Large
- Last WG meeting took place Feb. 11-12
- Modelers plan to submit manuscripts for phase 1 to peer-reviewed scientific journal this month

Smallpox Modeling Working Group

- Is surveillance & containment (ring vaccination) a valid strategy to contain a smallpox outbreak?
- How do additional measures affect outbreak control?
- Three modeling groups were selected
  - Dr. John Glasser
    - CDC
  - Drs. Betz Halloran and Ira Longini
    - Emory School of Public Health
  - Drs. Don Burke and Joshua Epstein
    - Johns Hopkins SPH & Brookings Institution

Outbreak Scenarios

- Scenario 1 (small)
  - 10 adult cases from an aerosol release in a restaurant, in a town of 5,000-6,000 people
- Scenario 2 (medium)
  - 500 mixed (adult and children) cases from an aerosol release in a movie-theater, in a town of 48,000-50,000 people
- Scenario 3 (large)
  - 10,000 mixed cases from an aerosol release in a sports stadium, in a town of ~ 1.6 million people

Standardized Parameters

- Distribution of disease
  - Ordinary, modified, hemorrhagic
- General population structure
  - Reflects most recent Census data
- Vaccine efficacy
- Characteristics of disease
  - Progression
  - Infectiousness
  - Behavior of infected people

Outbreak Control Measures Examined:

- Background immunity
- “Surveillance and containment” – also known as “ring vaccination”
  - identify and isolate cases, vaccinate close contacts…
- Pre-emptive vaccination of hospital staff
- School closure
- Reactive mass vaccination

It was also assumed that…

- Surveillance and containment would always implemented
- Patients would be effectively isolated when hospitalized
- Health-care workers with direct patient contact would be vaccinated immediately upon the recognition of an outbreak

Outcome Measures

- Total number of cases
- Proportion of cases within hospitals
- Number of persons vaccinated
- Duration of epidemic

Scenario 2 – 500 mixed cases in a population of 48,000-50,000 persons

–Surveillance & Containment strategy appears to be effective

Control Measures	Emory	Hopkins/ Brookings	CDC
Isolation in home or hospital	1750	-	1546
Plus surveillance & containment (S&C)	828	1492	1347
S&C plus 50% of HS vaccinated pre-emptively	678	1494	1347
Above plus schools closure for 10 days, and 40% post-event community vaccination*	367	1100	1205
As above, but 80% post-event community vaccination*	203	771	1089

* Within1 day of outbreak detection, over 7 days

Smallpox Modeling: Interim Conclusions

- The strongest controlling factor is people being hospitalized or withdrawing to the home when they become ill.
- There is relatively small marginal benefit in outbreak control through pre-vaccination of hospital workers.
- Mass vaccination of the population after an outbreak begins augments the effectiveness of other control measures.

Anthrax

- WG first met on October 2-3, 2003
- Last WG occurred April 8, 2004
- The aim is to reexamine HHS's current policy on the consequence management of a moderate to large-scale bioterrorist attack employing anthrax
- Evaluate alternative policy strategies
- Assess the impact of antibiotics, post-vaccination and pre-vaccination on the number of casualties

Modelers

- Dr. Ron Brookmeyer – JHU
- Dr. Larry Wein – Stanford
- Dr. Michael Boechler – IEM
- Dr. Nathaniel Hupert – Cornell
- Dr. John Glasser, CDC & Dr. Ellis McKenzie, FIC – to provide peer review

Scenario

- Large-scale
- Line source release in large metropolitan city
- 1 kg of dry-fill with a concentration of 10^{11} spores/g
- Population from most recent Census data
- Results in 1,391,886 people exposed

Policy Options

- Antibiotics
- Post-exposure vaccine with antibiotics
- Pre-exposure vaccine

Policy Options

1. Post-exposure prophylaxis with antibiotics x 60 days

2. Vaccine at 0, 2, 4 wks (vaccine distribution starts at 7 days after the beginning of antibiotic distribution) and antibiotics for 60 days

3. Vaccine at 0, 2, 4 wks and antibiotics for 10 days beyond completion of vaccine series

4. Pre-existing vaccine-induced immunity (10-80%) and each of the above or antibiotics for 60 days only for those who are not pre-immunized

Critical Factors and Outcome Measures of Interest

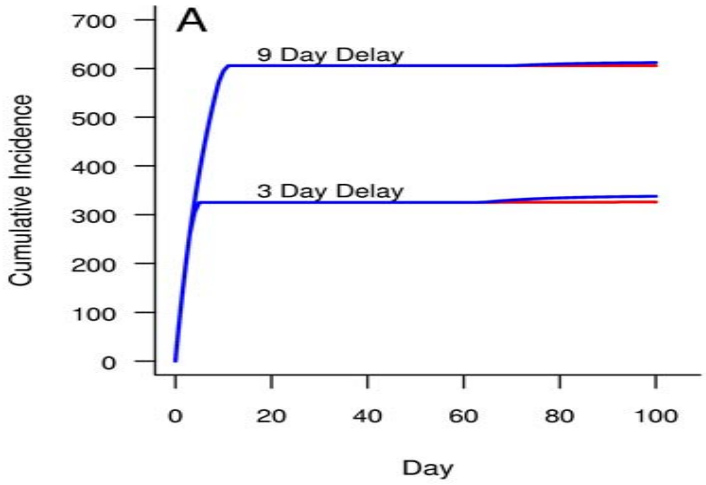
- Incubation period
- Time to detection
- Duration of time to distribute antibiotics
- Antimicrobial and vaccine efficacy
- Antimicrobial adherence
- Available hospital and emergency resources
- Effect of ‘worried-well’

- Number of cases and fatalities

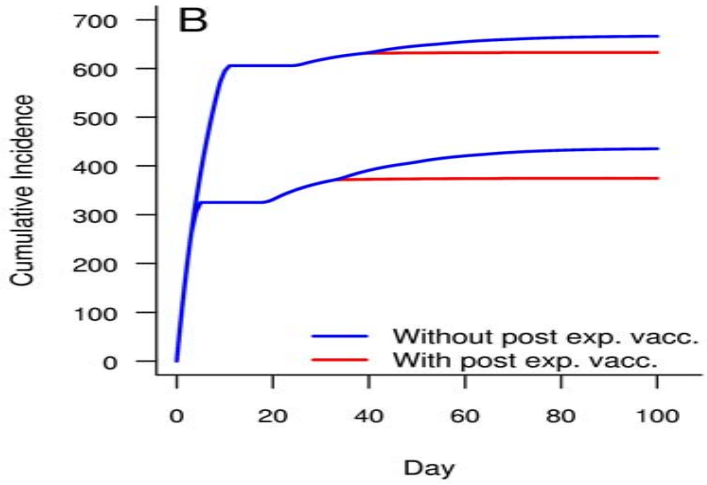
IMPACT OF POST EXPOSURE VACCINE

Variable dose scenario (cases/ 10,000)

Complete AB adherence



Partial AB adherence



VARIABLE DOSE SCENARIO; 60 DAYS AB; RAPID POST- EXP VACCINE
PARTIAL ADHERENCE WITH 25% EACH COMPLETING 15, 30, 45 AND 60 DAYS

Anthrax Modeling Interim Conclusions

- Antibiotics
  - Minimize delays in initiation and distribution
  - 60 days may not be sufficient for those exposed to high inocula
- Post-exposure vaccination
  - Important strategy in the setting of poor adherence
  - May shorten prolonged antibiotic courses (especially important in those exposed to high inocula), and spare antibiotics
  - May be important in reoccupation of contaminated areas
- Pre-exposure vaccination
  - Need high levels of coverage to have the same impact as 60 days of antibiotics
  - In the event of an antibiotic-resistant strain, no other alternative
  - Optimal if post-response systems are inadequate to respond in a short-period of time

Data Gaps Identified

- We need more data on spore clearance from lungs
- Effectiveness of antibiotics and vaccine in relation to inoculum
- Human dose-response curves
- Plume models in a complex environment, such as a cit
- Effective building protective factors
- Vaccine efficacy in different populations
- Duration of immunity
- Pre-clinical diagnostic testing
- Medical surge capacity

Plans underway to remediate “large lacunae in our knowledge”

Anthrax Modeling: Next Steps

- Harmonize input parameters
- Sensitivity testing
  - Vaccine efficacy
  - Time to achieve immunity
  - Duration of immunity
  - Incubation period
  - Dose-response curves

In summary:

- DHHS is bringing policy makers, scientists with subject matter expertise, and modelers to the table to address “a limited set of decision-oriented questions about intervention strategies following the introduction of a particular agent”
- The primary purpose of DHHS modeling efforts is to evaluate response strategies
- DHHS also hopes to use models to assist in the determination of requirements and options for biodefense countermeasures

- Modeling is not a predictive tool
- Modeling is a valuable tool to:
  - Systematically compare different policy strategies
  - Determine the most crucial issues in decision-making
  - Identify critical gaps in current knowledge

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